

REMARKS

I. Detailed Action

A. Election/Restrictions

The Examiner states that restriction to one of the following inventions is required under 35 U.S.C. § 121. Group I consists of claim 1, drawn to a viral immunogen. Group II consists of claims 73-77, drawn to a method of producing an immunogenic composition. The Examiner acknowledges that during a telephone conversation with Heidi Nebel on September 18, 2002 a provisional election was made with traverse to prosecute the invention of Group II, claims 73-77. Applicants herein affirm this election, with traverse, of Group II, claims 73-77. Applicants further submit an affirmation of this election was previously made on September 18, 2002 in a Response to Restriction Requirement on September 18, 2002.

B. Status of the Claims and Application

Applicants acknowledge that claims 73-77 are examined in the instant application. Applicants further acknowledge that claim 1 is non-elected. The Examiner acknowledges the receipt of Applicants' Preliminary Amendment filed March 23, 2001.

C. Oath/Declaration

The Examiner states that the oath or declaration is defective because the date of execution for the signature of Inventor Arntzen is missing. Applicants respectfully submit that according to MPEP § 602.05:

"The Office no longer checks the date of execution of the oath or declaration and the Office will no longer require a newly executed oath or declaration based on an oath or declaration being stale (that is when the date of execution is more than 3 months prior to the filing date of the application) or where the date of execution has been omitted. However, applicants are reminded that they have a continuing duty of disclosure under 37 C.F.R. § 1.56."

In addition, Applicants submit "[A] continuation or divisional application filed under 37 C.F.R. § 1.53(b) (other than a continuation-in-part (CIP)) may be filed with a copy of the oath or declaration from the prior nonprovisional application." See 37 C.F.R. § 1.63(d)(1)(iv). Therefore, Applicants respectfully submit this rejection be withdrawn as a copy of the properly signed declaration from the parent application identifying this application by application number and filing date was submitted.

D. Specification

Applicants acknowledge after careful reading of the Specification that several minor spelling and punctuation mistakes were found. The specification has now been amended to correct these minor changes that do not add new matter.

II. Double Patenting

Claim 73-77 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2 and 8-14 of U.S. Patent No. 5,612,487. Claims 73-77 also stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 9 of U.S. Patent No. 6,034,298. The Examiner states that although the conflicting claims are not identical, they are not patentably distinct from each other.

Applicants are herein submitting a Terminal Disclaimer in compliance with 37 C.F.R. § 1.321(c), which disclaims any term of a patent issuing from this application which would extend beyond the term of U.S. Patent No. 5,612,487 and U.S. Patent No. 6,034,298. Therefore, Applicants submit that the claims are in proper form for allowance and respectfully request reconsideration and withdrawal of the obviousness-type double patenting rejections.

III. Rejections – 35 U.S.C. § 112, Second Paragraph

Claims 73-77 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The Examiner states that in claim 73, "to said viral immunogen" should be inserted after "response" to clarify that the observed response is not something else. Applicants have now amended claim 73 to read --an immunogenic response to said viral immunogen--. Applicants thank the Examiner for pointing out this inadvertent mistake.

Claim 75 stands rejected for the recitation "chimeric protein" as it is unclear whether the components which make up the protein are chimeric to each other, or whether the protein is chimeric to the plant cell. Applicants respectfully traverse this rejection. Applicants assert

the specification states, "[T]he recombinant immunogens of the invention may represent the entire amino acid sequence of the native immunogen of the virus from which it is derived. However, in certain embodiments of the invention, the recombinant immunogen may represent only a portion of the native molecule's sequence. In either case, the immunogen may be fused to another peptide, polypeptide or protein to form a chimeric protein. The fusion of the molecules is accomplished either post-translationally through covalent bonding of one to another (e.g., covalent bonding of plant produced hepatitis B viral immunogen with whole hen egg lysozyme) or pre-translationally using recombinant DNA techniques (see e.g., supra discussion of poli virus vaccines), both of which methods are known well to those of skill in the art" (page 9, lines 17-25, specification). Applicants submit it would be clear that the components which make up the protein are chimeric to each other as stated in the specification, therefore, Applicants submit this term is clear and request withdrawal of the rejection to claim 75.

The Examiner states that claims 76 and 77 are unclear for the recitation "derived from" as it is unclear what is retained in the derived product. Applicants respectfully traverse this rejection. The specification states "[T]he immunogen of the invention is one derived from a mammalian virus and which is then expressed in a plant" (page 8, lines 6-8). Applicants assert claims 76 and 77 specifically claim the particular virus the immunogen is being derived from. In addition, the specification further teaches "the antigenic/immunogenic protein of the invention will be a protein known to be antigenic/immunogenic when the protein as derived from the native virus, mammalian or from standard pharmaceutical expression systems, is used to induce the immune response through an oral mode of introduction" (pages 7-8, lines 34-36 and 1-2, respectively). Applicants submit one ordinarily skilled in the art would understand the term "derived from" to mean an immunogen being derived from a particular virus whereby the virus possesses an antigen capable of eliciting an immune response and thereby the derived product retains the antigen, as taught by the specification. Applicants respectfully submit this ground of rejection is now alleviated.

Applicants respectfully assert all the claims are now in a condition for allowance. Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

IV. Claim Rejections - 35 U.S.C. § 102(b)

Claims 73-76 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Goodman et al., U.S. Patent No. 4,956,282. The Examiner states that Goodman teaches a method comprising expressing a recombinant viral immunogen in a plant, an immunogen capable of generating an immunogenic response when the immunogen interacts with a mucosal membrane, a chimeric protein comprising the protein of interest and a heterologous transit peptide, and an immunogen obtained from a hepatitis virus. The Examiner further states the oral administration limitation is an intended use and thus has no patentable weight in a method-of-making claim.

Applicants respectfully traverse this rejection. The Goodman et al. reference simply provides a general disclosure of a means of expressing mammalian peptides in plant cells. Goodman et al. does not teach the use of viral antigenic proteins expressed in transgenic plants or the use of the proteins as a vaccine which elicit an immune response upon oral administration. Applicants respectfully submit that “for prior art to anticipate under 35 U.S.C. § 102, every element of the claimed invention must be identically disclosed, either expressly or under principles of inherency in a single reference.” *Corning Glass Works v. Sumitomo Electric*, 9 U.S.P.Q.2d 1962, 1965 (Fed. Cir. 1989). The exclusion of a claimed element, no matter how insubstantial or obvious, from a prior art reference is enough to negate anticipation. *Id.* In order to be anticipated there must be a teaching of a viral, as opposed to bacterial or mammalian protein, properly folded (glycosylated) and finally that it expresses at adequate levels. *Ex parte Deuel*, 33 U.S.P.Q.2d 1445, 1451 (Bd. Pat. App. & Int’f 1993). This teaching cannot come from Applicants’ own specification. *Id.*

In addition, the general rule of inherency is that it may be relied upon where and only where the consequences of following the references disclosure always inherently produces a result in the claimed invention. If there is not a reasonable certainty that the claimed subject

matter will necessarily result, the rejection fails. See, *W.L. Gore Associates, Inc. v. Garlock, Inc.*, 220 U.S.P.Q. 303, 314 (Fed. Cir. 1983). Instead, there must be a teaching or suggestion within the prior art to combine the particular elements as done by the inventor. Therefore, Applicants submit that Goodman et al. clearly does not anticipate claims 73-76 because the prior art does not teach (1) a transgenic plant expressing a recombinant viral antigen protein; (2) whereby this protein is antigenic to a human or an animal following administration of this protein either in an isolated purified form or as an ingestible transgenic plant or plant component.

This reference can be clearly distinguished from the present application where a recombinant viral antigenic protein has been demonstrated to elicit an immune response when expressed in plant tissue and subsequently fed to animals to form antibodies. Goodman et al. provides a general disclosure of a means of expressing mammalian peptides in plant cells to achieve high yields which may be harvested (col. 1, line 41, lines 64-67). For example, the reference merely teaches the transformation of a dicotyledonous plant cell with a structural gene coding for an interferon whereby the interferon gene is expressed and harvested (col. 10, lines 39 and 50). The cited reference does not teach a specific means for expressing immunogen derived from a viral protein in a plant nor the administration of the claimed oral vaccine by consumption of the edible transgenic plant (page 7, specification). One skilled in the art would not expect membrane bound proteins as in the present invention, which are plagued with low expression levels, to be useful or determinable by Goodman et al. In fact, Goodman et al. at best contemplates the opposite, high production of recombinant mammalian proteins for harvesting only. Whereas the present application teaches expression of a viral protein which involves different mechanisms and concerns than expression of a mammalian protein in plants because a virus relies upon its host for proper expression and processing of the proteins produced. Goodman et al. does not discuss or teach how one might accomplish this result.

Further Goodman et al. does not teach an antigenic response in animals upon oral administration of tissue obtained from the claimed invention's transgenic plants. Goodman et al. only teaches the production of mammalian proteins and harvesting of such proteins for

later “integration of the construct into the plant genome under conditions where cells can be used to produce plants” (col. 2, lines 4-6). In contrast, the present invention clearly teaches the expression of viral derived antigenic proteins in tomato plants, and the ability to elicit an immune response in an animal or human when ingested (page 24, specification). However, Goodman et al. merely teaches the transformation of tobacco with interferon whereby the interferon gene is expressed. Goodman et al. also does not teach the use of viral antigenic proteins expressed in transgenic plants or the use of the proteins as a vaccine to these same viruses or the administration of the vaccine to elicit an immune response.

The Examiner has not shown a teaching in the cited art that the vectors and/or methods used in expressing mammalian proteins in transgenic plants could be used successfully with Applicants’ specific viral proteins. Moreover, it is well known in the art that while viruses rely on their host for proper processing, mammalian proteins are not only chemically different but also have their own processing mechanisms. The only means by which one of ordinary skill in the art could obtain the recombinant animal viral antigen protein, vaccines, and transgenic plants of claims 73-76 is through the use of impermissible hindsight reconstruction. At most, Goodman et al. is an invitation for one skilled in the art to attempt to express viruses in plants. However, it does not teach one skilled in the art the appropriate vectors, promoters, mediums, infection procedures, etc. to obtain viral immunogens derived from a hepatitis virus in a plant that are capable of producing a vaccine without an undue amount of experimentation. Thus, Goodman et al. does not provide sufficient description to one skilled in the art to practice the Applicants’ invention.

In light of the above, Applicants submit that the present invention is clearly distinguished from and, therefore, not anticipated by Goodman et al. Applicants respectfully request reconsideration and withdrawal of the rejections to claims 73-76 under 35 U.S.C. § 102(b).

V. Claim Rejections - 35 U.S.C. § 103(a)

Claims 73-77 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Goodman et al. (*supra*), as applied to claims 73-76 above, and further in view of Sanchez et

al. (*Virology*, vol. 190, pages 92-105, 1992). The Examiner states that although Goodman does not teach an immunogen obtained from a Transmissible Gastroenteritis Virus, Sanchez teaches a Transmissible Gastroenteritis Virus (TGEV) immunogen.

Applicants respectfully traverse this rejection. The cited references do not teach or suggest the claimed invention's plant derived recombinant viral antigens, anti-viral vaccines and transgenic plants expressing the same. As stated previously, Goodman et al does not teach the use of plants to express viral immunogens. Rather the reference simply provides a general disclosure of a means of expressing mammalian peptides in plant cells. Goodman et al. merely teaches the transformation of tobacco with interferon whereby the interferon gene is expressed. Goodman et al. does not teach or suggest the use of TGEV or HBsAg antigenic proteins expressed in transgenic plants or the use of the proteins as a vaccine to these same viruses.

Further, Sanchez et al. does not even begin to teach or suggest the claimed invention. In contrast, Sanchez et al. teaches the "genetic relationship among six European PRCVs and five coronaviruses of the TGEV antigenic cluster" (abstract). The reference discusses the analysis of the structural proteins of seven new strains of the TGEV cluster with enteric and respiratory tropism, the complete sequences of the S genes of three respiratory isolates and of the first 1956-nt S gene of other four respiratory viruses of the TGEV antigenic cluster (See page 101, col. 2).

Applicants submit there is no basis in the cited art for combining or modifying the cited references in the manner in which the Examiner has attempted. The Examiner is reminded that obviousness cannot be established by combining the teachings of prior art to produce a claimed invention, absent some teaching, suggestion or incentive supporting the combination. See *ACS Hospital Systems, Inc. Montefiore Hospital*, 221 U.S.P.Q. 929, 933 (Fed. Cir. 1984); *In re Geiger*, 2 U.S.P.Q.2d at 1278 (Fed. Cir 1987). Further, Applicants assert the prior art cited by the Examiner, in fact, teaches away from the current invention, a per se demonstration of lack of prima facie obviousness. In addition, both the suggestion and the expectation of success must be found in the prior art, not in the Applicants' disclosure. See *In re Dow Chemical Co.*, 837 F.2d 469 (Fed. Cir. 1988). Applicants strongly assert that

neither the suggestion of the claimed unique invention or any expectation of success is taught in the references cited by the Examiner.

Applicants submit that the combination of Goodman et al. in view of Sanchez et al. does not teach, or suggest the unique combination of elements of the present invention. At best, these references may provide a suggestion to try. However, obvious to try is not a proper standard for obviousness. "Selective hindsight is no more applicable to the design of experiments than it is to the combination of prior art teachings." *In re Dow Chemical Co.*, 837 F.2d 469 (Fed. Cir. 1988). In light of the above remarks, Applicants respectfully request reconsideration and withdrawal of the rejections to claims 73-77 under 35 U.S.C. § 103(a).

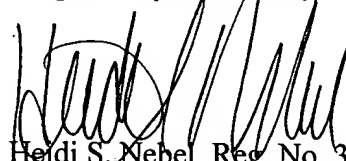
VI. Conclusion

In light of the above remarks, Applicants respectfully assert that claims 73-76 are now in condition for allowance. Applicants respectfully request reconsideration and withdrawal of the above rejections.

A request for a three-month extension of time is being submitted in connection with this amendment; however, please consider this a request for any additional extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,



Heidi S. Nebel, Reg. No. 37,719
McKEE, VOORHEES & SEASE
801 Grand Avenue, Suite 3200
Des Moines, Iowa 50309-2721
Phone No. (515) 288-3667
Fax No. (515) 288-1338
CUSTOMER NO: 22885

-LA/pw-

Attorneys of Record



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Jennell
Disclaim

PATENT
Attorney Docket: P00245USE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT : Arntzen, et al.
SERIAL NO : 09/816,846
FILED : March 23, 2001
TITLE : VACCINES EXPRESSED IN PLANTS

Grp./A.U. : 1638
Examiner : HELMER, Georgia L.
Conf. No. : 7468
Docket No. : P00245USE

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TERMINAL DISCLAIMER TO OBVIATE AN
OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTION
OVER A PRIOR PATENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Madam:

The owner, Prodigene, Inc., of 100 percent interest in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application, which would extend beyond the expiration date of the full statutory term defined in 35 U.S.C. §§ 154 to 156 and 173, as presently shortened by any terminal disclaimer, of prior U.S. Patent No. 5,612,487 and U.S. Patent No. 6,034,298. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the prior patents are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

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CERTIFICATE OF MAILING

I hereby certify that this document and the documents referred to as enclosed therein are being deposited with the United States Postal Service as First Class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, on this 1st day of April, 2003.

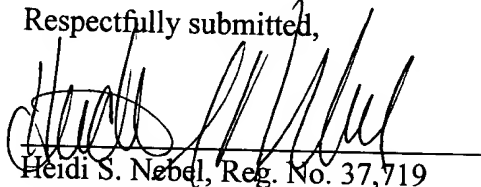
Heldi S. Nebel

In making the above disclaimer, the owner does not disclaim the terminal part of any patent granted on the instant application that would extend to the expiration date of the full statutory term as defined in 35 U.S.C. §§ 154 to 156 and 173 of the prior patents, as presently shortened by any terminal disclaimer, in the event that it later: expires for failure to pay a maintenance fee, is held unenforceable, is found invalid by a court of competent jurisdiction, is statutorily disclaimed in whole or terminally disclaimed under 37 C.F.R. § 1.321, has all claims canceled by a reexamination certificate, is reissued, or is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.

The undersigned is an attorney of record.

Enclosed please find a check in the amount of \$55.00 to cover the fee for a terminal disclaimer under 37 C.F.R. § 1.20(d). If this amount is incorrect, please charge any deficiencies or credit any overpayment to Deposit Account No. 26-0084.

Respectfully submitted,



Heidi S. Næbel, Reg. No. 37,719
McKEE, VOORHEES & SEASE
801 Grand Avenue, Suite 3200
Des Moines, Iowa 50309-2721
Telephone 515-288-3667
Facsimile 515-288-1338
CUSTOMER NO. 22885

-pw/LA-

Attorneys of Record